

Claims

1. A method for preparing (S)-indoline-2-carboxylic acid methyl ester by use of a hydrolytic enzyme, comprising the following steps:
 reacting racemic indoline-2-carboxylic acid with methanol and thionyl chloride, to give racemic indoline-2-carboxylic acid methyl ester;
 selectively hydrolyzing (R)-form of the racemic indoline-2-carboxylic acid methyl ester in a buffer solution by use of the hydrolytic enzyme to produce (S)-indoline-2-carboxylic acid methyl ester; and
 separating and recovering the (S)-indoline-2-carboxylic acid methyl ester, wherein said hydrolytic enzyme is selected from the group consisting of Savinase, Alcalase, Novozym 243, Everlase, Esperase, Protease 7, and Acylase.
2. The method as defined in claim 1, wherein the buffer solution is an aqueous sodium carbonate solution, and is maintained in pH 7 to 9.
3. The method as defined in claim 1, wherein the selective hydrolyzing step is performed at 25 to 50 °C for 3 to 85 hours.
4. The method as defined in claim 1, wherein a ratio by weight of the hydrolytic enzyme to the racemic indoline-2-carboxylic acid methyl ester is in a range of 1:10 to 1:40.
5. The method as defined in claim 1, wherein the concentration of the racemic indoline-2-carboxylic acid methyl ester ranges from 10 to 50% (w/w) in the selective hydrolyzing step.
6. The method as defined in claim 1, wherein the hydrolytic enzyme takes the form of powder or liquid, or forms immobilized on a support.
7. The method as defined in claim 1, wherein the recovered (S)-indoline-2-carboxylic acid methyl ester has an optical purity of at least 99 %e.e.
8. A method for preparing (S)-indoline-2-carboxylic acid by use of a hydrolytic enzyme, comprising the following steps:
 reacting racemic indoline-2-carboxylic acid with methanol and thionyl chloride, to give racemic indoline-2-carboxylic acid methyl ester;
 selectively hydrolyzing (R)-form of the racemic indoline-2-carboxylic acid methyl ester in a buffer solution by use of the hydrolytic enzyme to obtain an un-hydrolyzed (S)-indoline-2-carboxylic acid methyl ester;
 separating and recovering the (S)-indoline-2-carboxylic acid methyl ester; and

hydrolyzing the recovered (S)-indoline-2-carboxylic acid methyl ester in an alkali aqueous solution to produce (S)-indoline-2-carboxylic acid, followed by recovering the resulting (S)-indoline-2-carboxylic acid, wherein, said hydrolytic enzyme is selected from the group consisting of Savinase, Alcalase, Novozym 243, Everlase, Esperase, Protease 7, and Acylase.

9. The method as defined in claim 8, wherein the buffer solution is an aqueous sodium carbonate solution, and is maintained in pH 7 to 9.

10. The method as defined in claim 8, wherein the selective hydrolyzing step is performed at 25 to 50 °C for 3 to 85 hours.

11. The method as defined in claim 8, wherein a ratio by weight of the hydrolytic enzyme to the racemic indoline-2-carboxylic acid methyl ester is in a range of 1:10 to 1:40.

12. The method as defined in claim 8, wherein the concentration of the racemic indoline-2-carboxylic acid methyl ester ranges from 10 to 50% (w/w) in the selective hydrolyzing step.

13. The method as defined in claim 8, wherein the hydrolytic enzyme takes the form of powder or liquid, or forms immobilized on a support.

14. The method as defined in claim 8, wherein the recovered (S)-indoline-2-carboxylic acid has an optical purity of at least 99 %e.e.